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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,417	YASUDA ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claim 1 is cancelled. Claims 2-6 and 8-10 are amended. Claims 11-25 are newly submitted. Claims 2-25 are under current examination.

Priority

This application claims benefit as a 371 of PCT/JP05/05480 (filed 03/25/2005). This application also claims benefit from foreign patent applications JAPAN 2004-093417 (filed 03/26/2004) and JAPAN 2004-124524 (filed 04/20/2004). The instant application has been granted the benefit date, 26 March 2004, from the application JAPAN 2004-093417.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, second paragraph

Applicant's arguments, see page 13 and Claim amendments, filed 9 October 2007, with respect to claims 1-7 and 10 have been fully considered and are persuasive. The rejections of Claims 1-7 and 10 under 35 USC 112, second paragraph, have been made moot by the claim amendments (and claim 1 cancellation) submitted on 9 October 2007 and are hereby withdrawn.

Response to Arguments – Written Description (35 USC 112, first paragraph)

Applicant's arguments (pages 13-17) filed 9 October 2007 have been fully considered and they are persuasive.

Claim 1 has been cancelled and Claim 11 has been added as a replacement base claim. In making these claim amendments, the applicant has addressed the aspect of the written description rejection related to the breadth of organisms encompassed by a "transformant" by narrowing the scope of the claims to "transformant of *E. coli* or *Lactobacillus reuteri*." The examiner believes this amendment sufficiently narrows the scope of the claims to matter which is described in the specification.

The examiner also withdraws the portion of the written description rejection directed to the genus of genes identified by hybridization, because the base claim 1 has been cancelled.

Therefore, the rejection of claims 1-10 under 35 USC 112, first paragraph (written description) is hereby withdrawn.

Response to Arguments – ENABLEMENT (35 USC 112, first paragraph)

Applicant's arguments (pages 17-19) and claim amendments filed 9 October 2007 have been fully considered and they are persuasive.

Claim 1 has been cancelled and therefore the rejection is moot.

Therefore, the rejection of claims 1-7 and 10 under 35 USC 112, first paragraph (lack of enablement) is hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 102

Applicant's arguments (pages 19-22) and claim amendments filed 9 October 2007 have been fully considered and they are persuasive.

As claim 1 has been cancelled, the rejection of claims 1-5 and 10 under 35 USC 102(b) as anticipated by Dobrogosz et al. (US-5,352,586, issued October 4, 1994) is moot. Therefore, the examiner hereby withdraws this rejection.

As claim 1 has been cancelled, the rejection of claims 1 and 10 under 35 USC 102(b) as anticipated by Skraly et al. (US-6,329,183, issued 11 December 2001) is moot. Therefore, the examiner hereby withdraws this rejection.

Response to Arguments - Claim Rejections 35 USC § 103

Applicant's arguments (pages 22-25) and claim amendments filed 9 October 2007 have been fully considered and they are persuasive.

As claim 1 has been cancelled, the rejection of claims 1- 10 under 35 USC 103(a) as obvious over Dobrogosz et al. (US-5,352,586, issued October 4, 1994) in view of Skraly et al. (US-6,329,183, issued 11 December 2001) and as evidenced by Omura et al (US2006/0063217) is moot.

Therefore, the examiner hereby withdraws this rejection.

NEW GROUNDS OF REJECTION

Claim Objections

Claims 2-10 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claims 2-10 do not further limit a preceding claim. Rather they further limit a subsequent claim (claim 11).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION

Claims 11 and 14-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement;* (Federal Register/Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claims 11 and 14-25 are broadly drawn, such that they apply to a genus of *E.coli* and *Lactobacillus reuteri* transformants comprising nucleic acids that hybridizes under high stringency (see claims 15, 17, 19, 21, 23 and 25) to various genes (glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase). Claims 14, 16, 18, 20, 22, and 24 are directed to a genus of *E.coli* and *Lactobacillus reuteri* transformants comprising nucleic acids that encode proteins derived from a variety of amino acid sequences by deletion, substitution, or addition of 1-3 amino acid residues. As all the above-mentioned claims depend from Claim 11, it is clear that claim 11 also encompasses the scope specifically claimed in claims 14-25.

The specification tries to define genes through hybridization with known sequences. The specification defines the genes for glycerol dehydratase by

hybridization under stringent conditions (page 5). The specification defines the genes for propanol dehydrogenase by hybridization under stringent conditions (page 6). The specification defines the genes for propionaldehyde dehydrogenase by hybridization under stringent conditions (page 9). The specification defines the genes for propionate kinase by hybridization under stringent conditions (page 9). The specification defines the genes for 1,3-propanediol oxidoreducatase by hybridization under stringent conditions (page 13). However, the working examples provided in the instant application only demonstrate specific nucleic acids from *Lactobacillus reuteri.*

Whether defined by homology through hybridization or as a sequence derived from deletion, substitution or addition of amino acid residues, there is considerable breadth to the sequences which are encompassed by the instant claims. The specification does not state which amino acid substitutions and deletions are particularly being claimed. While the claims do recite that the resulting proteins have specific activity (e.g. – propionate kinase activity in the case of claim 24), the specification does indicate which amino acids can be deleted or substituted while maintaining this activity. It is well known in the art that even single amino acid changes can affect the functional activity of an enzyme. Because the specification does not explain which amino acids are contemplated as being part of the genus which contains the amino acid deletions or substitutions and yet also maintain functional enzyme activity, the examiner concludes that the claimed genus is not adequately described such that a skilled artisan would recognize that the applicant was in possession of the claimed genus of *E.coli* and *Lactobacillus reuteri* transformants comprising nucleic acids that encode proteins

derived from a variety of amino acid sequences by deletion, substitution, or addition of 1-3 amino acid residues. Furthermore, because the instant claims directed to nucleotide sequences that hybridization under stringent conditions also has a large breadth and the specification does not make a link between the specifically claimed function and uncertainly claimed structure, the examiner likewise concludes that the specification does not adequately described the claimed genus of *E.coli* and *Lactobacillus reuteri* transformants comprising nucleic acids that hybridizes under high stringency.

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page

1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Considering the potentially large numbers organisms comprising genetic mutations of polynucleotides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed. In addition, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed genus of "transformants" and "knockout bacteria" commensurate to its scope at the time the application was filed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Ahrne et al. (Current Microbiology. 1992 Vol. 24: 199-205).

Claim 11 is directed to transformants of *E.coli* or *Lactobacillus reuteri* comprising genes encoding large medium, and small subunits of glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase and large and small subunits of reactivation factors for glycerol dehydratase. The genes for propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase are intrinsic to the microorganism, *Lactobacillus reuteri,* since the endproducts of anaerobic glycerol metabolism are 1,3-propanediol and/or β-hydroxypropionic acid.

Ahrne et al. teach a "transformation system...developed for *Lactobacillus reuteri*" (abstract). Since all of the enzymes described in claim 11 are intrinsic to the organism, *Lactobacillus reuteri*, the only limitation seems to be transformation of *Lactobacillus reuteri* cells. Ahrne et al. clearly meet this limitation.

Therefore, Ahrne et al. anticipated the instant claim.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 10-11 and 2-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Laffend et al. (US-7,135,309, issued 14 November 2006). Claim 11 is directed to transformants of *E.coli* or *Lactobacillus reuteri* comprising genes encoding large medium, and small subunits of glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase and large and small subunits of reactivation factors for glycerol dehydratase. The genes for propanol dehydrogenase (claim 4), glycerol dehydratase (claim 2 and 5), propionaldehyde dehydrogenase (claim 11), propionate kinase (claim 6), glycerol dehydrogenase (claim 6), and 1,3-propanediol oxidoreducatase (claim 3) are intrinsic to the microorganism, *Lactobacillus reuteri,* since the endproducts of anaerobic glycerol metabolism are 1,3-propanediol and/or β-hydroxypropionic acid. Claim 10 is directed to a method of producing 1,3-propanediol and/or β-hydroxypropionic acid by culturing the transformants of claim 11 in glycerol and purifying 1,3-propanediol and/or β-hydroxypropionic acid. Laffend et al. teach, "It has bee known for over a century that 1,3-propanediol can be produced from the fermentation of glycerol...in...Lactobacillus." (col.1, lines 34-40). Laffend et al. teach, "Cells suitable in the present invention comprise those that harbor a dehydratase enzyme...[t]ypically the enzyme will be either a glycerol dehydratase or a diol dehydratase...includ[ing] mutated or recombinant organisms belonging to the genera... *Lactobacillus*....Other cells suitable as hosts in the present invention include *Escherichia* (col.13, lines 26-52). In example 24, Lactobacillus reuteri was cultured in

the presence of glycerol (claim 10) and 1,3-propanediol is implicitly purified by GC-MS and HPLC analysis of the cultured media (col.50, lines 13-37), satisfying the method of claim 10. In addition, Laffend et al. teach that their organisms can contain the pdu operon (claim 7).

Therefore, Laffend et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-7 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skraly et al (US-6,329,183, issued 11 December 2001) in view of Dobrogosz et al (US-5,352,586, issued October 4, 1994) .

Claims 11 and 2-5 are directed to transformants of *E.coli* and/or *Lactobacillus reuteri* comprising genes encoding large medium, and small subunits of glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase and large and small subunits of reactivation factors for glycerol dehydratase. Claims 2-5 further limit claim 11, by requiring that the genes be derived from *Lactobacillus reuteri.* Claim 3 specifies that the gene encoding propanol dehydrogenase is 1,3-propanediol oxidoreducatase from *Lactobacillus reuteri.* The instant specification describes a transformant as comprising nucleic acids that hybridizes under high stringency to various genes (glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase). Neither the claims nor the specification specifically define the term "transformant" as a recombinant microorganism. Furthermore, the claims do not specify a vector, plasmid, or homologous recombination as a part of the "transformant." Since the commonly understood meaning of "transformant" within the art is "a cell into which foreign DNA has been introduced" the examiner will broadly construe the claims in light of this definition. Furthermore, the specification indicates that reactivation factors for glycerol dehydratase or diol dehydratase include gdrA, gdrB, pduG, pduH, ddrA, ddrB, dhaF,

dhaG, orfZ, and orfY (page 14, lines 5-6). In addition, the specification indicates that *Lactobacillus reuteri* inherently contains genes encoding subunits of reactivation factors for glycerol dehydratase or diol dehydratase.

Dobrogosz et al. teach, *Lactobacillus reuteri* comprising the genes for glycerol dehydratase (col.2, lines 61-62). The genes for propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase are intrinsic to the microorganism, *Lactobacillus reuteri,* since the endproducts of anaerobic glycerol metabolism are 1,3-propanediol and/or β-hydroxypropionic acid. Dobrogosz et al. teach culturing *Lactobacillus reuteri* in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42).

Claim 10 is directed to a method for producing 1,3-propanediol and/or 3-hydroxypropionic acid from culturing a recombinant microorganism in the presence of glycerol. Dobrogosz et al. teach culturing Lactobacillus reuteri in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42).

Claim 11 is directed to *E.coli* and/or *Lactobacillus* transformants having various genes encoding glycerol dehydratase, propanol dehydrogenase, propionaldehyde dehydrogenase, propionate kinase, and 1,3-propanediol oxidoreducatase. Skraly et al. teach, "organisms that contain one or both dehydratases typically are able to convert glycerol to 3-hydroxypropionaldehyde to 1,3-propanediol" (col.5, lines 57-59) and "Because all the genes necessary to implement the production of poly(3-hydroxypropionate) from central metabolic intermediates via glycerol have been cloned and are available in genetically manipulatable for, any combination of plasmid-borne

and integrated genes may be used and the implementation of this pathway is therefore not restricted to the schemes outlined herein. Many different implementations will be apparent to those skilled in the art." (col.5, lines 40-47).

Claim 10 is directed to a method for producing 1,3-propanediol and/or 3-hydroxypropionic acid from culturing a recombinant microorganism in the presence of glycerol. Skraly et al. teach "transgenic *Escherichia coli* synthesized...1,3-propanediol from glycerol" (col.7, lines 14-15). Skraly et al. also teach, "genetically engineered systems for the production...of 1,3-propanediol from glycerol" (col.6, lines 44-46).

Skraly et al. does not teach the source of the genes cited in claims 2-5 as coming from *Lactobacillus reuteri.*

Skraly et al., however, teach, "Because all the genes necessary to implement the production of poly(3-hydroxypropionate) from central metabolic intermediates via glycerol have been cloned and are available in genetically manipulatable for any combination of plasmid-borne and integrated genes may be used and the implementation of this pathway is therefore not restricted to the schemes outlined herein. Many different implementations will be apparent to those skilled in the art." (col.5, lines 40-47). Dobrogosz et al. list a variety of bacteria including *Lactobacillus* and *Escherichia* (col.9).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to culture recombinant bacteria in glycerol to produce 1,3-propanediol and/or 3-hydroxypropionic acid, using a variety of possible enzymatic alternatives in a variety of possible microorganisms.

The person of ordinary skill in the art would have been motivated to make those modifications because 1,3-propanediol and/or 3-hydroxypropionic acid are "industrially useful as polymers or as starting materials for a range of chemical intermediates " (Skraly, abstract).

The skilled artisan would have had a reasonable expectation of success in combining the teachings of Skraly et al. and Dobrogosz et al. because each of these references teach production of 1,3-propanediol and/or β-hydroxypropionic acid from glycerol using microorganisms. Dobrogosz et al. teach culturing Lactobacillus reuteri transformants in glycerol to produce 1,3-propanediol and/or β-hydroxypropionic acid (col.12, lines 40-42). Skraly et al. teach "transgenic *Escherichia coli* synthesized...1,3-propanediol from glycerol" (col.7, lines 14-15).

Therefore the method as taught by Skraly et al. in view of Dobrogosz et al. would have been *prima facie* obvious over the method of the instant application.

Claims 8-9 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nair et al. (US-7,005,291, issued 28 February 2006).

Claim 8 is directed to a knockout bacteria of *Lactobacillus reuteri* comprising lacking glycerol dehydrogenase activity by knocking out the gene encoding glycerol dehydrogenase. Claim 9 is directed to a similar organism as claim 8, except that the *Lactobacillus reuteri* must also contain the pdu Operon and a gene encoding

phosphotransacylase. Nair et al. teach, "recombinant host having disruptions in genes encoding endogenous glycerol dehydrogenase enzymes (col.5, lines 13-16). Nair et al. teach, "glycerol dehydrogenase protein, the produce of gldA, is produced in the [E.coli] transformants.... Of 8 transformants analyzed, 6 were determined to be gldA knockouts" (col.24, lines 55-67). *Lactobacillus reuteri* inherently contains the Phosphate acetyltransferase gene and pdu operon.

Claims 12 and 13 are directed to methods of producing 1,3-propanediol and/or β-hydroxypropionic acid, using the knockout bacteria of claims 8 and 9, respectively. Nair et al. teach a "process...for a recombinant organism...in a host cell having disruptions in the endogenous ...dehydrogenase genes...[a]pplicant's process may generally applied to the production [of] compounds where glycerol is a key intermediate, e.g., 1,3-propanediol" (col.5, lines 23-30).

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to use the teachings of Nair et al. to generate a Lactobacillus reuteri comprising a knocked out phosphotransacylase gene in order to produce compounds where glycerol is a key intermediate, e.g., 1,3-propanediol.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (recombinant microorganisms comprising knocked out

phosphotransacylase gene; recombinant production of 1,3-propanediol by recombinant host having disruptions in genes encoding endogenous glycerol dehydrogenase enzymes) are taught by Nair et al.

Therefore the method as taught by Nair et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JLE